Hepatobiliary Excretion Scintigraphy Revisited

TO REDUCE THE MORBIDITY AND MORTALITY associated with acute cholecystitis, the diagnosis must be made or excluded in any patient seen because of right upper quadrant abdominal pain occurring suddenly. Ultrasonography is the procedure of choice in diagnosing the presence of gallstones, although a stone lodged in the cystic or common bile duct may often be missed. Furthermore, the presence of cholelithiasis of itself does not imply acute cholecystitis. Cholescintigraphy using technetium Tc 99m iminodiacetic acid is a sensitive and accurate examination for the presence of acute cholecystitis and biliary duct obstruction because in 98% of patients acute cholecystitis is caused by obstruction of the cystic duct.

The principal scintigraphic sign of acute cholecystitis is nonfilling of the gallbladder within an hour in spite of normal hepatic excretion, which has a false-positive rate of as high as 10% to 12% because of chronic cholecystitis, pancreatitis, nonfasting (less than 2 hours), prolonged fasting (greater than 12 hours), the use of total parenteral nutrition, alcoholism, hepatocellular disease, and severe intercurrent illness. It is claimed that the false-positive rate can be reduced by taking delayed views as much as four hours later. One study has shown that not only can the rate of false-positive results be reduced to 2% but the total study time can be reduced to an hour by administering intravenous morphine sulfate (0.04 mg per kg body weight) after 30 to 40 minutes when the gallbladder is not visualized and small bowel activity has excluded common duct obstruction. The sphincter of Oddi contracts and raises the intrabiliary pressure. Administering 2.5 mg of intravenous morphine has been shown to nearly double bile duct pressure (12.7 to 20.0 cm of saline). The maximum effect takes place about five minutes after the injection. It has been postulated that the increase in bile duct pressure may be enough to overcome partial or functional obstruction of the cystic duct and thereby raise the incidence of false-positive results. Nevertheless, it is now generally accepted that morphine-augmented cholescintigraphy is a safe and sensitive means of diagnosing acalculous and calculous cholecystitis.

Cholecystokinin and sincalide (0.02 μg per kg) can be used to empty viscous bile from the gallbladder as seen in patients with prolonged fasting and total parenteral nutrition. The radiopharmaceutic agent is given 30 minutes after injection during the gallbladder filling phase. This procedure can also be used to contract a visualized gallbladder to test common bile duct patency. In one study common bile duct obstruction was detected in 63 of 65 patients, for a positive predictive value of 97%. The two false-positive results were caused by cholangitis of an undetermined origin. Sonographic evaluation alone, however, has a high false-negative rate of 63%. It is usually wise to exclude by sonography the presence of small biliary stones that could be dislodged into the common duct.

Neonatal hepatitis can be differentiated from biliary atresia by administering phenobarbital, 2.5 mg per kg twice per day for three to seven days, to stimulate biliary secretion before administering 1 mCi (37 megabecquerels [MBq]) of ^{99m}Tc tracer. Intestinal activity seen within 24 hours in a jaundiced infant is probably due to neonatal hepatitis or prolonged hyperalimentation. A lack of intestinal activity in this time period suggests biliary atresia. The sensitivity for detecting biliary atresia is high, approaching 100% in several series. The specificity has been reported from 47% to 63% without pretreatment with phenobarbital to 63% to 94% with pretreatment.

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Captopril Renograms for Detecting Renovascular Hypertension

RENOVASCULAR HYPERTENSION occurs in about 1% of people in the general population having hypertension. Those with intermediate risk factors have prevalence rates of about 5%. Rates as high as 31% occur in persons with severe hypertension. Hence, the sensitivity and specificity of any screening test for renovascular hypertension must be greater than 90%. Until now, standard tests have not met these criteria, nor have they been shown to be practical for screening. Because the presence of renal artery stenosis does not necessarily imply the presence of renovascular hypertension, the arteriographic demonstration of renal artery stenosis in a hypertensive person is not equivalent to a diagnosis of the disorder. Furthermore, renal artery stenosis, although frequent and more severe among hypertensive patients, occurs without an associated elevation of blood pressure. The ability to identify renovascular hypertension is important because it is amenable to surgical correction and a subsequent reduction of the blood pressure, leading to a decreased rate of hypertension-related disease and death.

Renovascular hypertension characteristically is dependent on increased renin secretion by the juxtaglomerular apparatus of an underperfused stenotic kidney. Renin acts by increasing the production of angiotension II, both a potent vasoconstrictor and a stimulator of aldosterone secretion by the adrenal cortex, prompting an increased resorption of sodium and water in the distal convoluted tubule. Glomerular filtration is maintained in the affected kidney by the vasoconstrictive action of angiotensin on the efferent arteriole. Captopril, an angiotensin-converting enzyme inhibitor, counteracts this vasoconstrictive effect, causing release of the constricting action on the efferent arteriole and a reduction in glomerular filtration. Because this effect can only be shown in patients with renovascular hypertension and not in those with essential hypertension, captopril is being used in radioisotope renography to document this effect and thus the presence of the renovascular disorder. The radioisotope renogram, as a diagnostic tool for renovascular hypertension, has in the past had a sensitivity and specificity of 80% to 85%, which are not significantly better than those of the rapid-sequence intravenous pyelogram, largely because of renal diseases such as chronic pyelonephritis, obstruction, or parenchymal disease that mimic the findings. Captopril renography has become most useful in distinguishing those

abnormalities that are caused by the renin-angiotensin-aldosterone effects of the disorder from those that are not.

Standard renal function evaluation techniques that use either technetium Tc 99m pentetic acid (DTPA) (excreted by glomerular filtration) or iodohippurate sodium I 131 or I 123 (excreted primarily by tubular secretion) show a delayed transit time through the kidney and therefore a prolonged excretory phase that results from the renin effect of reducing urine flow on the affected side. When captopril is administered before these tests, there is a substantial drop in the glomerular filtration rate. This affects the ^{99m}Tc-DTPA renogram by dropping the rate of tracer accumulation and the iodohippurate renogram by delaying the transit time (time to peak) and excretion rate half-time owing to the altered dynamics. These changes are not noted in essential hypertension where there is either an increase or no significant change in the glomerular filtration rate. In patients with renovascular hypertension with severely reduced renal function, the magnitude of the change may be reduced, making the test less sensitive. In those with complete renal artery stenosis, although renin production is increased, there is no handling of these radiopharmaceuticals as is to be expected. In nearly complete stenosis, there is also no demonstrable captopril effect, but an iodohippurate study does show the classic retention pattern. In mild stenosis (<50%) there is neither increased renin production nor a captopril effect.

Although large-scale studies using captopril in this manner have not yet been done, the well-defined mechanistic response to angiotensin inhibition should significantly enhance the 80% to 85% sensitivity of standard renograms in identifying renovascular hypertension and differentiating it from essential hypertension and other renal diseases.

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Dacryoscintigraphy Revisited

NASOLACRIMAL DUCT OBSTRUCTION is a frequent cause of epiphora (excess tearing). A diagnostic evaluation is required to rule out other common causes of epiphora such as lower lid horizontal laxity or conjunctival inflammation. A proper diagnosis is essential because the traditional treatment of nasolacrimal duct obstruction is surgical correction. Recently a new technique has been described that uses a balloon catheter—like doing coronary angioplasty—to dilate the nasolacrimal duct. This has stimulated a renewed interest in a physiologic assessment of nasolacrimal duct patency.

Two office procedures may be done to evaluate nasolacrimal duct obstruction: irrigation of the lacrimal system and dye testing. Nasolacrimal duct obstruction may be diagnosed when there is complete obstruction to irrigation of the lacrimal system at the level of the nasolacrimal duct. In many patients with epiphora, however, there is no physiologic drainage of tears through the nasolacrimal duct, but forceful irrigation through the nasolacrimal duct may be accomplished (functional nasolacrimal duct obstruction). Functional nasolacrimal duct obstruction may be diagnosed by placing fluorescein dye in the eye and a cotton swab in the nose to recover the dye. This test has been criticized as unreliable because of problems recovering the dye in the nose of some patients.

The tearing process was first studied with radioisotopes in 1973. A major difference between a radionuclide dacryocystogram and an x-ray contrast dacryocystogram is that the radionuclide study is physiologic and better depicts the natural flow of tears. The study consists of placing a drop of technetium Tc 99m pertechnetate in the conjunctival space and imaging the passage of the labeled tears into the nose. X-ray dacryocystography, on the other hand, requires canalization of the nasolacrimal duct and the administration of contrast using pressure, which can mask the anomaly.

Recently 16 patients were studied before balloon dilatation of the nasolacrimal duct. In each case the dacryoscintigram showed the obstruction. In addition, the site of obstruction along the nasolacrimal path was found and the degree of obstruction was apparent. Dacryoscintigraphy is thus a useful diagnostic test to evaluate patients with epiphora and suspected functional nasolacrimal duct obstruction.

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Radiolabeled Monoclonal Antibodies for Detecting and Treating Cancer

THE USE OF MONOCLONAL ANTIBODIES offers a new procedure, called immunoscintigraphy, for detecting and treating cancer. The basic concept is to use monoclonal antibodies as a carrier to transport the radionuclide to the tumor sites, using the mechanism of the binding of antibody to the site of antigen. When antibodies are labeled with γ-ray-emitting radionuclides, such as technetium Tc 99m and others, they can be used to detect primary and metastatic lesions. The antibodies can also be labeled with β-ray-emitting radionuclides such as iodine 131 and others and be applied for treatment.

Radioimmunoscintigraphy is successfully used to detect solid tumors including melanoma; hepatocellular carcinoma; neuroblastoma; carcinomas of the breast, prostate, colorectum, lung, and ovary; and nonsolid tumors such as B-cell and T-cell lymphomas. In our experience, ^{99m}Tc-anti-melanoma antibody provides excellent quality diagnostic imaging with a high tumor-to-soft-tissue ratio. Besides the known lesions that have been identified, there are many unexpected lesions detected with this radiolabeled antibody and later confirmed to be metastatic melanoma lesions. Because of the need to alter treatment plans, the clinical importance of detecting unexpected sites cannot be overemphasized. This melanoma antibody is currently under the review of the Food and Drug Administration and is expected to be approved this year. Other antibodies such as those of lymphoma, breast cancer, lung cancer, colorectal, and prostate cancer are in the